



MINISTRY OF AGRICULTURE, FISHERIES AND FOOD

**FOOD ADDITIVES AND
CONTAMINANTS COMMITTEE
SECOND REPORT ON
CYCLAMATES**



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Food Additives and Contaminants Committee

The terms of reference of the Food Additives and Contaminants Committee are:

To advise the Minister of Agriculture, Fisheries and Food, the Secretary of State for Scotland, the Minister of Health, and as respects Northern Ireland, the Secretary of State for the Home Department, on matters referred to them by Ministers, in relation to food contaminants, additives and similar substances which are or may be present in food, or used in its preparation, with particular reference to the exercise of powers conferred on Ministers by Sections 4, 5 and 7 of the Food and Drugs Act, 1955 and the corresponding provisions in enactments relating to Scotland and Northern Ireland.

The members of the Food Additives and Contaminants Committee are:

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Pharmacology Sub-Committee

The terms of reference of the Pharmacology Sub-Committee are:

To advise at the request of the Committee on Medical Aspects of Food Policy, the Food Additives and Contaminants Committee, the Ministry of Agriculture, Fisheries and Food, the Ministry of Health, the Scottish Home and Health Department, or the Ministry of Health and Social Services, Northern Ireland on the hazard to health, including toxicological and carcinogenic risks, resulting from the use or presence of additives or contaminants in or on food.

The members of the Pharmacology Sub-Committee are:

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FOOD ADDITIVES AND CONTAMINANTS COMMITTEE

Second Report on Cyclamates

Further evidence on Cyclamates

1. We were asked to consider further additional evidence on cyclamates (in particular the results of metabolic studies^{(1) (2)}) which has become available since our report dated November 1965. The report of the Pharmacology Sub-Committee which is attached at Appendix I re-affirms that a daily intake of 50 mg. cyclamates/kg. body weight should not be exceeded and asks for further work to be done to elucidate the significance of cyclohexylamine excretion in relation to the metabolism of cyclamates.

Conclusions

2. We have carefully considered whether the new evidence calls for any change in our recommendations. We have noted that all the evidence at present available indicates that the toxicity of cyclohexylamine is low.

3. We have also considered again whether the acceptable daily intake of 50 mg. cyclamates/kg. body weight is likely to be exceeded. In Paragraph 7 of the Pharmacology Sub-Committee's first report (Appendix I to our report of November 1965) some estimates were given of the upper limits of consumption of cyclamates. These have been examined in conjunction with the fact that cyclamates cannot be a substitute for sugar in its nutritional, culinary and preservative functions; they only replace the sweetening effect. In practice, therefore, cyclamates tend to be used to replace saccharin rather than sugar and furthermore cyclamates are often used in combination with saccharin.

Recommendations

4. We re-affirm the recommendations in our first report and we endorse the recommendations in the second report of the Pharmacology Sub-Committee. In addition we consider that, pending the development of a revised specification in accordance with the Pharmacology Sub-Committee's recommendation, the cyclohexylamine content of cyclamates should not exceed 100 p.p.m.

Summary of Conclusions and Recommendations of the two Reports

5. (1) There would be no risk to health in allowing the use of cyclamates without statutory limitation except for that already laid down in the Soft Drinks Regulations, 1964. (First Report, para. 3).

(2) There should be no amendment to the ban on the use of artificial sweeteners in ice-cream. (First Report, para. 4).

(3) Any regulations made as a result of these reports should be reviewed five years after the date of making. (First Report, para. 5).

(4) Pending the development of a specification for cyclamates in accordance with the Pharmacology Sub-Committee's recommendations, the cyclohexylamine content of cyclamates should not exceed 100 p.p.m. (Para. 4 above).



(5) Work should be done on the following lines:—

- (i) a study of the physiological and biochemical mechanism of the laxative effect (Pharmacology Sub-Committee First Report, para. 15);
- (ii) long-term feeding studies on a second species (e.g. the mouse), and injection tests on rats, the results to be available within 5 years (Pharmacology Sub-Committee First Report, para. 15);
- (iii) a full toxicological examination of cyclohexylamine, including adequate metabolic studies in man and rats, to be completed within three years (Pharmacology Sub-Committee Second Report, Appendix I, para. 4(a));
- (iv) further metabolic studies on cyclamates, to be completed within five years (Pharmacology Sub-Committee Second Report, Appendix I, para. 4(b));
- (v) a revised specification for cyclamates (Pharmacology Sub-Committee Second Report, Appendix I, para. 4(c)).

References

- (1) B.I.B.R.A. Bulletin; 1966, 5, 615 and 669.
- (2) Unpublished information from the Huntingdon Research Centre (1967).

FAC/REP/6

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REPORT OF THE PHARMACOLOGY SUB-COMMITTEE

Cyclamates and Cyclohexylamine

1. The Pharmacology Sub-Committee was requested to consider new evidence on the metabolism of cyclamates which had become available since their last report to the Food Additives and Contaminants Committee on 16th September, 1965.
2. It has been reported in one study that 5 out of 40 persons ingesting cyclamates for 2 to 3 days excreted, on average, about 0.8 per cent of the dose as cyclohexylamine while after administration for 17 days the percentage of ingested cyclamates converted to cyclohexylamine rose in one person to 7.5 per cent. No dicyclohexylamine was detected in the urine after ingestion of cyclamate. The results of studies on cyclamates administered to guinea pigs which were carried out at an Austrian Physiological Institute were also considered.
3. If the Pharmacology Sub-Committee had been in possession of this information at the time of their original consideration of cyclamates they would have requested the carrying out of further work necessary to resolve these problems raised by the finding of cyclohexylamine as a metabolite of cyclamates in man. However the Pharmacology Sub-Committee did not feel that the further evidence submitted was sufficient to alter their earlier recommendations on the level of the daily intake of cyclamates by man. They emphasised that this level had been based on the premise of metabolic inertness, and on the fact that a possible laxative action was the only side effect. The recent finding that cyclamates are metabolised by some people led them to re-affirm their opinion that a daily intake of 50 mg/kg. body weight should not be exceeded.
4. Furthermore, the Sub-Committee considered that the Food Additives and Contaminants Committee should be made aware that in their opinion the following requirements should be added to those enumerated in their earlier report:
 - (a) cyclohexylamine should be fully examined from the toxicological point of view within the next three years as a matter of urgency, with particular emphasis on adequate metabolic studies in man and rats;
 - (b) within five years further metabolic studies on cyclamates should be carried out to elucidate the relationship to cyclohexylamine excretion; and
 - (c) the specification of cyclamates should be revised to include satisfactory methods for the quantitative detection of cyclohexylamine and the related dicyclohexylamine and to set acceptable limits for these impurities.

